DOCKET NO. 701586/50113-C

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Sabanayagam et al.

Application No.: Unassigned Group No.:

Filed: Herewith Examiner:

FOR: NUCLEIC ACID ARRAYS AND METHODS OF SYNTHESIS

Assistant Commissioner for Patents
Washington, DC 20231

****

CERTIFICATE OF MAILING

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Date: 6/21/01 Patricia W. Turner
Patricia W. Turner

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PRELIMINARY AMENDMENT

Applicants are submitting simultaneously herewith a new continuation application. Please amend the following application as follows:

IN THE SPECIFICATION:

On page 1, before line 1, please add the following:

--This application is a continuation of copending application 09,287,781, filed April 8, 1999, which is hereby incorporated by reference, which claims benefit of provisional application 60/081,254, filed April 9, 1998.

On page 1, line 5, after "Energy", insert -- and Contract No. DAAH04-95-1-0358 awarded by the Army Research Office --.

Page 10, line 18, after "QQQQetc.", delete “SEQ ID NO: 3”.

Page 11, line 5, after "interest", delete -- (SEQ ID NO: 3) --.

Page 11, line 8, after "DNA molecule", delete “SEQ ID NO: 2 followed by SEQ ID NO: 3 followed by SEQ ID NO: 4 followed by SEQ ID NO. 3” and insert therefor -- including a complementary sequence hybridizing with the immobilized oligonucleotide and the sequence of interest and --.

Page 11, line 14, after “WWWW” delete “(SEQ ID NO: 4)”.

Page 11, line 17, after "Figure 1A", delete “SEQ ID NO: 4”.

Page 11, line 25, delete “SEQ ID NO: 5” and insert therein --SEQ ID NO; 3--.

Page 11, line 26, after "QQQQetc.", delete “SEQ ID NO: 6”.

Page 12, line 10, after " DNA molecule," delete “SEQ ID NO: 5 followed by SEQ ID NO: 7 followed by SEQ ID NO:5 followed by SEQ ID NO:7 followed by SEQ ID NO:5 followed by SEQ ID NO:7” and insert therefor -- comprising one or more complementary sequences capable of hybridizing with the immobilized oligonucleotide which complementary sequences are separated by one or more separating regions --.

Page 12, line 14, after "WWWW", delete “W (SEQ ID NO: 7)”.

Page 15, line 6, after "P1", delete “SEQ ID NO: 8” and insert therefor --(SEQ ID NO: 4)--.

Page 15, line 6, after "P1", delete “SEQ ID NO: 8” and insert therefor --(SEQ ID NO: 4)--.

Page 15, line 7, after "T1", delete “SEQ ID NO: 9” and insert therefor --(SEQ ID NO: 5)--.

Page 15, line 7, after "T2", delete “SEQ ID NO: 10” and insert therefor --(SEQ ID NO: 6)--.

Page 16, line 11, after "P1", delete “SEQ ID NO: 8” and insert therefor --(SEQ ID NO: 4)--.

Page 16, line 11, after "P2", delete “SEQ ID NO: 11” and insert therefor--(SEQ ID NO: 7)--.

Page 16, line 13, after "T1", delete “SEQ ID NO: 9” and insert therefor --(SEQ ID NO: 5)--.

Page 16, line 13, after "T2", delete “SEQ ID NO: 10” and insert therefor --(SEQ ID NO: 6)--.

Page 16, line 18, after "A12", delete “SEQ ID NO: 12” and insert therefor - (SEQ ID NO: 8)--.

Page 17, line 13, after "5’FAACTAATACACCAA", delete “SEQ ID NO: 13” and insert therefor -- (SEQ ID NO: 9)--.

Page 23, line 25, after "GGC CCA AG", delete “SEQ ID NO: 14 and insert therefor --(SEQ ID NO: 10)--.

Page 23, line 26, after "X=Biotin", delete “SEQ ID NO: 15” and insert therefor --(SEQ ID NO: 11)--.

Page 26, line 20, after "P1", delete “SEQ ID NO: 8” and insert therefor --(SEQ ID NO: 4)--.

Page 26, line 21, after "T1", delete “SEQ ID NO: 9” and insert therefor --(SEQ ID NO: 5)--.

IN THE CLAIMS:

Please cancel claims 1-10, 12-22, and 24. Please amend the claims as follows:

11. An ordered redundant array of immobilized oligonucleotides produced by:

(a) providing: i) a solid support comprising a plurality of positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of identical oligonucleotides, each oligonucleotide comprising a sequence; and iii) a plurality of unique circular DNA templates, each circular DNA template comprising a sequence of interest and a region complementary to at least a portion of said sequence of said oligonucleotides, said sequence of interest being different for each circular template;

(b) immobilizing one oligonucleotide from said plurality of identical oligonucleotides in each of said positions on said solid support to create an ordered array comprising a plurality of identical immobilized oligonucleotides;

(c) adding to each immobilized oligonucleotide of said ordered array a circular DNA template from said plurality of said unique circular DNA templates under conditions such that said immobilized oligonucleotide hybridizes to said circular DNA template to create a plurality of primed circular templates, each primed circular template comprising a different sequence of interest; and

(d) extending each of said primed circular templates along a z coordinate to create an extended immobilized oligonucleotide comprising at least two copies of said sequence of

interest, thereby generating an ordered redundant array, wherein said ordered redundant array refers to said array having at least two copies of said sequence of interest along the z coordinate.

23. An ordered redundant array of immobilized oligonucleotides produced by:

a) providing: i) a solid support comprising positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of oligonucleotides, each oligonucleotide comprising a sequence complementary to a different portion of the sequence of said target nucleic acid; and iii) a plurality of corresponding circular DNA templates, each circular DNA template comprising a different portion of the sequence of said target;

b) immobilizing each of said oligonucleotides in one of said positions on said solid support to create an ordered array comprising a plurality of immobilized oligonucleotides;

c) adding to each immobilized oligonucleotide of said ordered array along a z coordinate a corresponding circular DNA template under conditions such that said immobilized oligonucleotide hybridizes to said corresponding circular DNA template to create a plurality of primed circular templates; and

d) extending said primed circular templates to create an ordered redundant array of extended immobilized oligonucleotides, each extended immobilized oligonucleotide comprising at least two copies of said portion of said sequence of said target nucleic acid, wherein said ordered redundant array refers to said array having at least two copies along the z coordinate of said portion of the sequence of interest contained in said primed circular template.

REMARKS

Attached hereto is an Appendix showing the changes made to claims 11 and 23.

Applicants have amended the specification to comply with the provisions of 35 U.S.C. §120. Applicants have also amended the specification to provide grant information. Finally, applicants have amend the specification to provide corrected SEQ ID numbers for the

nucleotides referred to therein. As such, these amendments do not constitute new matter and their entry is respectfully submitted.

In view of the foregoing amendment it is respectfully submitted that all claims are in condition for allowance. Early and favorable action is requested.

If any additional fee is required, charge Deposit Account No. 50-0850.

Respectfully submitted,

Ronald I. Eisenstein
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Date 6/21/01

Customer No. 26248

APPENDIX

The changes made by amendments to the claims are shown below with insertions being underlined and deletions being bracketed.

11. An ordered redundant array of immobilized oligonucleotides produced [according to the method of claim 1] by:

(a) providing: i) a solid support comprising a plurality of positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of identical oligonucleotides, each oligonucleotide comprising a sequence; and iii) a plurality of unique circular DNA templates, each circular DNA template comprising a sequence of interest and a region complementary to at least a portion of said sequence of said oligonucleotides, said sequence of interest being different for each circular template;

(b) immobilizing one oligonucleotide from said plurality of identical oligonucleotides in each of said positions on said solid support to create an ordered array comprising a plurality of identical immobilized oligonucleotides;

(c) adding to each immobilized oligonucleotide of said ordered array a circular DNA template from said plurality of said unique circular DNA templates under conditions such that said immobilized oligonucleotide hybridizes to said circular DNA template to create a plurality of primed circular templates, each primed circular template comprising a different sequence of interest; and

(d) extending each of said primed circular templates along a z coordinate to create an extended immobilized oligonucleotide comprising at least two copies of said sequence of interest, thereby generating an ordered redundant array, wherein said ordered redundant array refers to said array having at least two copies of said sequence of interest along the z coordinate.

23. An ordered redundant array of immobilized oligonucleotides produced [according to the method of claim 13] by:

a) providing: i) a solid support comprising positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of oligonucleotides, each oligonucleotide comprising a sequence complementary to a different portion of the sequence of said target

nucleic acid; and iii) a plurality of corresponding circular DNA templates, each circular DNA template comprising a different portion of the sequence of said target;

b) immobilizing each of said oligonucleotides in one of said positions on said solid support to create an ordered array comprising a plurality of immobilized oligonucleotides;

c) adding to each immobilized oligonucleotide of said ordered array along a z coordinate a corresponding circular DNA template under conditions such that said immobilized oligonucleotide hybridizes to said corresponding circular DNA template to create a plurality of primed circular templates; and

d) extending said primed circular templates to create an ordered redundant array of extended immobilized oligonucleotides, each extended immobilized oligonucleotide comprising at least two copies of said portion of said sequence of said target nucleic acid, wherein said ordered redundant array refers to said array having at least two copies along the z coordinate of said portion of the sequence of interest contained in said primed circular template.

ABSTRACT

The present invention generally relates to high density nucleic acid arrays and methods of synthesizing nucleic acid sequences on a solid surface. Specifically, the present invention contemplates the use of stabilized nucleic acid primer sequences immobilized on solid surfaces, and circular nucleic acid sequence templates combined with the use of isothermal rolling circle amplification to thereby increase nucleic acid sequence concentrations in a sample or on an array of nucleic acid sequences.

Practitioner's Docket No. 50113-C *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: C. Sabanayagam et al.
Application No.: To be assigned Group No.: 1655
Filed: Herewith Examiner: Lu, F.

For: NUCLEIC ACID ARRAYS AND METHODS OF SYNTHESIS

Box Sequence
Assistant Commissioner for Patents
Washington, D.C. 20231

TRANSMITTAL OF SUBSTITUTE SPECIFICATION SHEETS (37 C.F.R. § 1.125)

1. Enclosed are substitute specification sheets **31-40** for pages **31-36** of the originally filed specification in this application.

2.

[ ] This substitute specification is submitted, in response to a requirement by the Examiner. Namely, filing of SEQUENCE LISTING.

OR

[X] This substitute specification is being voluntarily submitted, in order to facilitate the processing of the application.

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Patricia W. Turner
Signature

Patricia W. Turner
(*type or print name of person certifying*)

3. As required by 37 C.F.R. § 1.125, the undersigned states that the substitute specification transmitted herewith contains no new matter.

SIGNATURE OF PRACTITIONER

Reg. No. 30,628

Ronald I. Eisenstein
(type or print name of practitioner)

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SEQUENCE LISTING

<110> SABANAYAGAM, Chandran R.
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MISASI, John
HATCH, Anson
CANTOR, Charles

<120> NUCLEIC ACID ARRAYS AND METHODS OF SYNTHESIS

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CLAIMS

We Claim:

1. ~~A method of generating an array, comprising:~~

a) providing: i) a solid support comprising a plurality of positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of identical oligonucleotides, each oligonucleotide comprising a sequence; and iii) a plurality of unique circular DNA templates, each circular DNA template comprising a sequence of interest and a region complementary to at least a portion of said sequence of said oligonucleotides, said sequence of interest being different for each circular template;

b) immobilizing one oligonucleotide from said plurality of identical oligonucleotides in each of said positions on said solid support to create an ordered array comprising a plurality of identical immobilized oligonucleotides;

c) adding to each immobilized oligonucleotide of said ordered array a circular DNA template from said plurality of said unique circular DNA templates under conditions such that said immobilized oligonucleotide hybridizes to said circular DNA template to create a plurality of primed circular templates, each primed circular template comprising a different sequence of interest; and

d) extending each of said primed circular templates to create an extended immobilized oligonucleotide comprising at least two copies of said sequence of interest, thereby generating an ordered redundant array.

2. The method of Claim 1, wherein said oligonucleotides are immobilized on a solid surface by a chemical linkage.

3. The method of Claim 1, wherein said oligonucleotides are immobilized on said solid surface by the 5' end of said oligonucleotides.

4. The method of Claim 1, wherein said oligonucleotides are approximately 17 bases in length.

~~5. The method of Claim 1 wherein said solid surface is selected from a~~ group of materials comprising silicon, metal, and glass.

6. The method of Claim 1 wherein said immobilized oligonucleotides are attached to a complimentary nucleic acid stabilizer sequence.

7. The method of Claim 1, wherein said circular nucleic acid template is bacteriophage DNA.

8. The method of Claim 1, wherein said circular nucleic acid template is non-bacteriophage DNA.

9. The method of Claim 1, wherein said extending in step (d) is achieved with a polymerase.

10. The method of Claim 9, wherein said polymerase is selected from a group comprising *E. coli.* DNA polymerase I, a fragment of *E. coli.* DNA polymerase I, or Φ29 DNA polymerase.

11. An ordered redundant array of immobilized oligonucleotides produced according to the method of Claim 1.

12. A method of hybridizing target nucleic acid fragments, comprising:

a) providing i) the ordered redundant array of extended immobilized oligonucleotides of Claim 1; and ii) a plurality of fragments of a ~~target nucleic acid; and~~

b) bringing said fragments of said target nucleic acid into contact with said array under conditions such that at least one of said fragments hybridizes to one of said extended immobilized oligonucleotides on said array.

13. A method of generating an array capable of hybridizing to fragments of a target nucleic acid, comprising:

a) providing: i) a solid support comprising positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of oligonucleotides, each oligonucleotide comprising a sequence complementary to a different portion of the sequence of said target nucleic acid; and iii) a plurality of corresponding circular DNA templates, each circular DNA template comprising a different portion of the sequence of said target;

b) immobilizing each of said oligonucleotides in one of said positions on said solid support to create an ordered array comprising a plurality of immobilized oligonucleotides;

c) adding to each immobilized oligonucleotide of said ordered array a corresponding circular DNA template under conditions such that said immobilized oligonucleotide hybridizes to said corresponding circular DNA template to create a plurality of primed circular templates; and

d) extending said primed circular templates to create an ordered redundant array of extended immobilized oligonucleotides, each extended immobilized oligonucleotide comprising at least two copies of said portion of said sequence of said target nucleic acid.

14. The method of Claim 13, wherein said oligonucleotides are immobilized on a solid surface by a chemical linkage.

15. The method of Claim 13, wherein said oligonucleotides are immobilized on said solid surface by the 5' end of said oligonucleotides.

16. The method of Claim 13, wherein said oligonucleotides are approximately 17 bases in length.

17. The method of Claim 13 wherein said solid surface is selected from a group of materials comprising silicon, metal, and glass.

18. The method of Claim 13 wherein said immobilized oligonucleotides are attached to a complimentary nucleic acid stabilizer sequence.

19. The method of Claim 13, wherein said circular nucleic acid template is bacteriophage DNA.

20. The method of Claim 13, wherein said circular nucleic acid template is non-bacteriophage DNA.

21. The method of Claim 13, wherein said extending in step (d) is achieved with a polymerase.

22. The method of Claim 21, wherein said polymerase is selected from a group comprising *E. coli.* DNA polymerase I, a fragment of *E. coli.* DNA polymerase I, or Φ29 DNA polymerase.

23. An ordered redundant array of immobilized oligonucleotides produced according to the method of Claim 13.

24. A method of hybridizing target nucleic acid fragments, comprising:

a) providing i) the ordered redundant array of extended immobilized oligonucleotides of Claim 13; and ii) a plurality of fragments of a ~~target nucleic acid; and~~

b) bringing said fragments of said target nucleic acid into contact with said array under conditions such that at least one of said fragments hybridizes to one of said extended immobilized oligonucleotides on said array.